REMARKS

Claims 9, 13-20 and 24 are rejected under 35 USC 101 because the claimed invention is not supported by a specific asserted utility or well-established utility. The Examiner states that the specification teaches general utility for the invention, not a specific utility. These claims have been canceled.

The Examiner states that further research would be required to identify a disease for which the protein encoded by SEQ ID NOS:1-14 is involved and for which treatment with SEQ ID NOS:1-14 or any nucleic acid having 90% identity with SEQ ID NOS:1-14 would be effective or for which detection of SEQ ID NOS:1-14 expression would be informative.

Applicant respectfully disagrees. The specification teaches that the claimed sequences express themselves more abundantly in breast tissue than any other tissue, thereby establishing that breast tissue is the host tissue of the claimed gene products.

Several assays utilizing the overexpression of tissue-specific gene products have been established in the art. The court has consistently stated that claim language must be read in light of prior art and teachings of the specification. The standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971).

Applicant has previously described how gene products that are expressed in a host tissue but not in other tissue can be used to indicate disease when they are found to be overexpressed in tissue outside their host tissue (e.g., CEA, PSA). Such overexpression indicates that a disease has altered the polynucleotides so that they escape from their host tissue (in this case breast tissue) into other areas of the body, such as blood. These examples demonstrate that presence of the claimed gene products outside normal host tissue serves as a diagnostic indicator that the host tissue is in a diseased state. Thus, the correlation of tissue-specific gene products, such as those claimed in the present invention, to disease states, such as cancer, are established in the art.

Applicant has also described previously how the RING finger family, of which the claimed gene product BS203 is a member, includes a variety of proteins with oncogenic proteins. These proteins, and their functions are known in the art (e.g., the breast cancer susceptibility gene BRCA1, the RET finger protein Rfp, the transcriptional intermediary factor TIF1, the Cb1 and Bmi-1 proto-oncogenes and Mel18 which is a nuclear DNA binding protein isolated from melanomas). Thus the correlation of RING finger family members, such as those claimed in the present invention, to disease states, such as cancer, are established in the art.

Because the claims should be analyzed in light of the teachings of the prior art and well-known techniques of immunohistochemistry for assessing overexpression are incorporated into the specification, Applicant asserts that the examples and methods disclosed in the specification are useful for detecting, at the least, breast diseases that may be detected using gene markers and related gene marker technology. Applicant respectfully submits that new claims 25-34 are now in a condition for allowance and requests that this rejection be withdrawn.

Applicant further reminds the Examiner that a protein or nucleic acid marker is useful not only for the direct detection of cancer in a biopsy sample but may also be useful in making a diagnosis or prognosis regarding the patient's disease status. Further, a protein or nucleic acid may not be present in high levels or at all in every tumor. For example, in the case of HER2-neu, only 1/3 of breast cancers overexpress this protein. Thus, in a breast cancer library, a very low level of HER2-neu will be present even though it is a very accurate breast cancer marker. Indeed, HER2-neu is used as a standard breast cancer marker.

Overexpression can be assessed by the well-known technique of immunohistochemistry using an antibody directed against the protein. For breast cancer patients with overexpression of HER-2-neu, treatment with Herceptin, a human-mouse chimeric antibody directed against the protein has therapeutic value. Also, if the gene which codes for HER-2-neu is amplified (multiple copies are present) as detected by the well known techniques of *in situ* hybridization, again the patient will likely respond to Herceptin treatment. However, if the patient does not exhibit an amplified gene or overexpression of the protein, treatment with Herceptin is unlikely to be of benefit.

Similarly, testing for estrogen receptor protein by immunohistochemistry is used as an indicator for treatment with anti-estrogens such as Tamoxifen. Only 2/3 of breast cancer patients express estrogen receptor in their tumors and thus benefit from Tamoxifen therapy. Based on the above, it is clear that the presence or absence of gene products that are expressed in the body is of diagnostic significance for cancer in a manner consistent with the methods and products claimed in new claims 25-34. Thus, the claimed polynucleotides of the present invention exhibit credible utility for several genres of tests well known in the art, whether direct or indirect in nature. Applicant respectfully submits that new claims 25-34 are now in a condition for allowance and requests that this rejection be withdrawn.

Claims 9, 13-20 and 24 are rejected under 35 USC 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. These claims have been canceled. Moreover, Applicant asserts that in light of the above amendments and remarks, the new claims are in a condition for allowance and requests that this rejection be withdrawn.

The Examiner states that "with respect to the breadth of the claims, the claims are inclusive of polynucleotide [sic] having at least 90% identity with SEQ ID NO:1-14. The claims further encompass polynucleotide [sic] which encode for at least one epitope.... [T]he claimed polynucleotide [sic] have been defined in the specification only in terms of the fact that they are BS203 polynucleotide [sic]." In an effort to expedite prosecution, claims 9, 13-20 and 24 have been cancelled. New claims 25-34 do not include "percent identity" language. New claims 25-34 are further clarified by "breast tissue-specific" language rather than BS203 language. Furthermore, new claims 25-34 encompass degenerate coding sequences thereof. The degeneracy of the genetic code is a concept that is well known to those skilled in the art and is even discussed in section 2144.09 of the February 2000 revision of the Manual for Patent Examining Procedure as "the fact that most amino acids are specified by more than one nucleotide sequence or codon." Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

The Examiner further states that "the specification does not identify any epitopes and no guidance is provided as to how one of skill in the art would select appropriate fragments of a protein which function as an epitope". Applicant seeks to clarify that methods for identifying epitopes in a novel peptide sequence are well known and described in both the scientific, commercial, and patent literature. For example, M. H. Van Regenmortel describes how to predict epitopes from the primary sequence of a protein. (See "Protein structure and antigenicity", *Int J Rad Appl Instrum B.*, **14(4)**:277-80, 1987.)

Further, Perkin-Elmer Biosystems, a major provider of DNA sequencing and peptide synthesizing instruments has established a public website which describes how to select peptides which reflect the epitopes of a protein. (See http://www.pebio.com/pa/340913/html/chapt2.html#Choosing the Epitope.) This electronic publication was posted in 1996 and basically describes the process employed by the inventors of the current patent application.

In addition, patent application PCT/US97/00485 describes in detail how to identify epitopes from peptide sequences. The sequence can be scanned for hydrophobicity and hydrophilicity values by the method of Hopp, Prog. Clin. Biol. Res. 172B: 367-377 (1985) or the method of Cease et al, J. Exp. Med. 164: 1779-1784 (1986) or the method of Spouge et al, J. Immunol. 138: 204-212 (1987). Commercial software programs to implement these methods are available.

In light of the above amendments and remarks, Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicant respectfully submits that the above-referenced application is now in a condition for allowance and Applicant respectfully requests that the Examiner withdraw all outstanding objections and rejections and passes the application to allowance.

Respectfully submitted,
M. Cohen, *et al.*

ABBOTT LABORATORIES
D-0377/AP6D-2
100 Abbott Park Road
Abbott Park, Illinois 60064-6050
Phone: (847) 935-7550
Fax: (847) 938-2623

Mimi C. Goller
Registration No. 39,046
Attorney for Applicants

CARDINAL LAW GROUP
1603 Orrington Avenue
Suite 2000
Evanston, Illinois 60201
Phone: (847) 905-7111
Fax: (847) 905-7113

Ruth Pe Palileo
Registration No. 44,277
Agent for Applicants